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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,393	01/12/2007	Patrick Holt	65138(53253)	9686

21874 7590 09/02/2009

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EXAMINER	
JUEDES, AMY E	
ART UNIT	PAPER NUMBER
1644	
MAIL DATE	DELIVERY MODE
09/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,393	HOLT ET AL.	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33,50 and 51* is/are pending in the application.

4a) Of the above claim(s) *2,9,11,12,14-18,20,22,23,25,26,30 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-8,10,13,19,21,24,27-29,31-33 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 March 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/30/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 4/22/09, is acknowledged.
Claims 34-49 have been cancelled.
Claims 3-8, 17-18, 20, 22-24, 27-29, and 32-33 have been amended.
Claim 51 has been added.
Claims 1-33 and 50-51 are pending.

2. Applicant's election with traverse of group I, drawn to a method of altering a specific immune response, claims 1-29, 31-33, and 51, in the reply filed on 4/30/09 is acknowledged. Applicant has further elected TH2 associated disease and TH1 adjuvant as the species of disease/adjuvant, respectively.

Applicant's traversal is on the grounds that it would not be an undue burden to examine the kit or agent of group II. This is not found persuasive because examination of the method claim of group I requires consideration of factors such as dosage, timing, and efficacy that are not necessarily relevant to product claims. Moreover, a search for the product of group II requires searching additional subject matter than the method of group I, since the product might have been used for a different purpose than the method of instant claims. Additionally, undue burden is irrelevant to the restriction practice for cases filed under 35 U.S.C 371 (see MPEP Chapter 1800).

The requirement is still deemed proper and is therefore made FINAL.

Claims 30 and 50 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 2, 9, 11-12, 14-18, 20, 22, 23, and 25-26 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species. It is noted that claims 2 and 22 are withdrawn since they are directed to administering an adjuvant that induces the type of Th response targeted during the immunotherapeutic step (i.e. administering a Th1 adjuvant for the immunotherapy of a Th1 immune response/disorder or administering a Th2 adjuvant for immunotherapy of a Th2 response/disorder). In contrast, Applicant has elected treating a Th2 disorder (i.e. performing the immunotherapeutic step to

reduce a Th2 response) with a Th1 adjuvant.

Claims 1, 3-8, 10, 13, 19, 21, 24, 27-29, 31-33, and 51 read on the elected invention and are being acted upon.

3. The drawings are objected to because the Y axis label is missing for Fig. 4. New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13, 21, 24, and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of treating allergic diseases including atopic dermatitis, allergic asthma and allergic rhinitis comprising administering an antigen in immunotherapeutic form followed by the antigen in immunogenic form,

does not reasonably provide enablement for:

A method of treating a Th2 associated disease, including hyper IgE syndrome and Omenn's syndrome, and a method of treating a disease comprising administering an antigen in immunotherapeutic form followed by the antigen in immunogenic form.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by

the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The instant claims are drawn to a method involving administration of an antigen in immunotherapeutic form, followed by administration of the same antigen in immunogenic form. The claims encompass performing the method to treat any disease, including Th2 associated diseases. Antigen administration in various immunotherapeutic forms is known in the art as a means of decreasing Th2 immune responses for treating antigen specific allergic reactions (see Drachenberg et al. and France et al.). However, the ability of antigen immunotherapy to treat any disease is highly unpredictable. For example, the claims might encompass treating infections or cancer, which would not be expected to benefit from a therapy that suppresses T cell responses. Additionally, the instant claims might encompass treating systemic lupus erythematosus (SLE), which is a disorder involving IL-4 mediated tissue damage (i.e. Th2 associated, see Singh, 2003). However, the instant specification discloses that the method of the claims results in a shift from aTh2 response to a Th1 response. Th1 cytokines, such as IFN-gamma are known to be a major effector molecule in the pathogenesis of SLE (see Theofilopoulus et al., 2001). Therefore, the treatment of the instant claims which increases Th1 cytokines would not be expected to be effective for

SLE. Furthermore, the instant claims specifically recite that the method is effective for treating Omenn's syndrome. Omenn's syndrome is a genetic deficiency leading to a global expansion of Th2 cells (see Villa et al., 2008). Standard treatment for Omenn's syndrome involves global immunosuppression and the ability of an antigen specific treatment, as recited in the instant claims, to treat such a disease would be highly unpredictable. In particular, an antigen specific therapy would only target a subset of Th2 cells, and the antigen specificity of the disregulated T cells is not known. Additionally, the instant claims specifically recite that the method is effective for treating hyper IgE syndrome. Hyper IgE syndrome is a result of various genetic deficiencies, one being a mutation in STAT3 (see Holland et al., 2007, in particular). Patients with hyper IgE syndrome have elevated levels of many Th1 cytokines and elevated IgE levels that are potentially due to defects in IL-21 receptor signaling (see Holland et al., page 11 in particular). Thus, a treatment that reduces Th2 cytokines while elevating Th1 cytokines, as is encompassed by the instant claims, would unlikely be effective in treating hyper IgE syndrome.

Thus, based on the unpredictability of the art and the breadth of the claims, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims. The specification demonstrates TH2 immune responses can be reduced by administration of an antigen by a sublingual, oral, or subcutaneous route (i.e. an "immunotherapeutic: form), followed by administration of the antigen by a different mechanism, including administration with adjuvant or intraperitonial administration (i.e. an "immunogenic" form). The specification demonstrates that this can result in a reduction of an allergic Th2 response to said antigen. However, no examples are provided relating to other Th2 disorders, other diseases, or genetic deficiencies such as hyper IgE syndrome or Omen's syndrome. Additionally, no guidance is provided with regard to antigen selection that would be effective for treating the diseases as broadly claimed. Thus, the teachings of the specification are not commensurate in scope with the instant claims. Based on the unpredictability of the art and the lack of guidance provided by the instant specification, it would require undue experimentation to practice the method as broadly claimed.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 3-6, 13, 19, 21, 24, 27-28, and 31-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Franco et al., 1998.

Franco et al. teach a method for reducing a Th2 immune response to an antigen (i.e. a method of treating an antigen specific allergic reaction) comprising administering an antigen via the oral route (i.e. in immunotherapeutic form) and subsequently administering the antigen in CFA by a subcutaneous injection (i.e. in immunogenic form comprising a Th1 adjuvant). Franco et al. teach performing the method in mice, which can be considered "livestock". Franco et al. teach administering 5 doses of the antigen via the oral route, and 1 dose of the antigen in CFA (see page 2, in particular). Franco et al. teach that the oral antigen is administered with a syringe and can thus be considered an "injection", see page 2 in particular). Franco et al. teach administering the antigen (DNP) attached to a carrier protein (i.e. an "agent" designed to modulate the specific immune response, see page 2 in particular). Additionally, the method of Franco et al. results in a reduction in a Th2 immune response to the antigen compared to an animal not receiving the oral antigen, and it can be considered a method of treating a Th2 mediated allergic response against said antigen. (i.e. an atopic disorder or disease) .

Thus, the reference clearly anticipates the invention.

7. Claims 1, 3-8, 10, 13, 19, 21, 24, and 27-29, are rejected under 35 U.S.C. 102(b) as being anticipated by Drachenberg et al., 2001.

Drachenberg et al. teach a method of immunotherapy for treating pollen specific allergy comprising administering low doses of pollen allergen and MPL adjuvant (i.e. an "immunotherapeutic" dose) followed by administration of high doses of pollen allergen

and MPL adjuvant (i.e. an "immunogenic" form of the antigen comprising a Th1 adjuvant, see page 500 in particular). Drachenberg et al. teach that the method functions by changing the T cell cytokine profiles from a Th2 to a Th1 type (see page 502, in particular). Drachenberg et al. teach performing the method in a human (i.e. a primate, see page 500 in particular). Drachenberg et al. teach including the MPL adjuvant in the lower doses (i.e. an immunotherapeutic form further comprising an agent designed to modulate the specific immune response). Drachenberg et al. teach administering several doses of the antigen (see page 500 in particular).

Thus, the reference clearly anticipates the invention.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-6, 13, 19, 21, 24, 27-28, 31-33 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Franco et al., 1998, in view of U.S. Patent Application Publication 2002/0173625, Nov. 2002.

The teachings of Franco et al. are discussed above.

Franco et al. do not teach administering the immunotherapeutic form of the antigen by a sublingual route.

The '625 publication teaches that administration by oral or sublingual routes is routinely used in immunotherapeutic treatments for allergy (i.e. for the reduction of Th2 responses (see page 2, in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to administer the immunotherapeutic form of the antigen by the sublingual route, as taught by the '625 publication, in the method of reducing a Th2 response taught by Franco et al. Selecting among the known routes for immunotherapy of Th2 response such as oral or sublingual would involve choosing among a finite number of predictable options which could be pursued with a reasonable expectation of success. A person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense (see *KSR International Co. V. Telefex Inc* 82 USPQ2d 1385).

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes whose telephone number is 571-272-4471. The examiner can normally be reached on 7am to 3:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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